Efficient Identification of Equivalences in Dynamic Graphs and Pedigree Structures

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Abstract

We propose a new framework for designing test and query functions for complex structures that vary across a given parameter such as genetic marker position. The operations we are interested in include equality testing, set operations, isolating unique states, duplication counting, or finding equivalence classes under identifiability constraints. A motivating application is locating equivalence classes in identity-by-descent (IBD) graphs, graph structures in pedigree analysis that change over genetic marker location. The nodes of these graphs are unlabeled and identified only by their connecting edges, a constraint easily handled by our approach. The general framework introduced is powerful enough to build a range of testing functions for IBD graphs, dynamic populations, and other structures using a minimal set of operations. The theoretical and algorithmic properties of our approach are analyzed and proved. Computational results on several simulations demonstrate the effectiveness of our approach.

Keywords: Hash Functions, Algorithms, Data Structures, Pedigree Analysis, Identity-by-Descent Graphs

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1 Introduction

In modern genetic analyses, we have genetic marker data $\mathbf{Y}_M$ on individuals available at multiple genetic markers across the genome, and the parameters of genetic marker models, $\mathbf{\Gamma}_M$, are generally well established. By contrast the models $\mathbf{\Gamma}_T$ underlying trait data are less clear. The goal of genetic linkage analyses is to locate DNA that affects the trait relative to the known locations of the genetic marker map. This requires computation of the conditional probability $\mathrm{P}(\mathbf{Y}_T \mid \mathbf{Y}_M\,;\,\mathbf{\Gamma})$, where $\mathbf{\Gamma}$ is a joint model comprising $\mathbf{\Gamma}_M$ and $\mathbf{\Gamma}_T$ and a specification γ of the relative genome locations of DNA underlying $\mathbf{Y}_M$ and $\mathbf{Y}_T$. This probability will be required for multiple specifications of the location of DNA affecting the trait, and may be required for multiple values of trait parameter values $\mathbf{\Gamma}_T$ and potentially for multiple trait phenotypes on the same sets of related individuals.

This key probability is most easily considered as

$$\mathrm{P}(\mathbf{Y}_T \mid \mathbf{Y}_M\,;\,\mathbf{\Gamma}) = \sum_{\mathbf{Z}} \mathrm{P}(\mathbf{Y}_T \mid \mathbf{Z}\,;\,\gamma,\mathbf{\Gamma})\,\mathrm{P}(\mathbf{Z} \mid \mathbf{Y}_M\,;\,\mathbf{\Gamma}_M) \tag{1}$$

where $\mathbf{Z}$ is an collection of latent variables insuring the conditional independence of $\mathbf{Y}_M$ and $\mathbf{Y}_T$ given $\mathbf{Z}$. Classically, the chosen latent variables $\mathbf{Z}$ were the unobserved genotypes (types of the DNA) of the individuals of the pedigree structure [Elston and Stewart, 1971, Lathrop et al., 1984]. More recently a specification of the inheritance of the DNA at all relevant locations has been the preferred choice of $\mathbf{Z}$ [Lander and Green, 1987, Lange and Sobel, 1991, Thompson, 1994]. On large pedigrees, with data at multiple marker locations, the probability in (1) cannot be computed exactly, especially if the data are sparse on the pedigree structures or if these structures are complex. Instead, realizations of $\mathbf{Z}$ from $\mathrm{P}(\mathbf{Z} \mid \mathbf{Y}_M\,;\,\mathbf{\Gamma}_M)$ are obtained. A Monte Carlo estimate of $\mathrm{P}(\mathbf{Y}_T \mid \mathbf{Y}_M\,;\,\mathbf{\Gamma})$ is the mean of the values of $\mathrm{P}\big(\mathbf{Y}_T \mid S^{(k)}\,;\,\gamma,\mathbf{\Gamma}_T\big)$ over the N realized $\big\{\mathbf{Z}^{(k)} : k = 1, ..., N\big\}$. Several effective MCMC methods have been developed to obtain these realizations [Sobel and Lange, 1996, Thompson, 2000, Tong and Thompson, 2008].

In the context of modern informative marker data, an efficient choice of $\mathbf{Z}$ is the pattern of gene identity by descent (IBD), across the chromosome, among individuals observed for the trait [Thompson, 2011]. This defines a graph, the IBD graph, which, at each locus, is analogous to the descent graph of [Sobel and Lange, 1996]. The edges of this graph are the observed individuals, and the nodes represent IBD sharing at this genome location among the edges (individuals) connecting to that node. The IBD graph is a deterministic function of the inheritance specification, and for marker genotypes Y_M observed without error, computation of the probability of these data for a given IBD graph is easy [Kruglyak et al., 1996, Sobel and Lange, 1996], Thus use of the IBD graph led to greater efficiencies in obtaining MCMC realizations from $\mathrm{P}(\mathbf{Z} \mid \mathbf{Y}_M\,;\,\mathbf{\Gamma}_M)$. However, it has been less well appreciated that computation of $\mathrm{P}\big(\mathbf{Y}_T \mid \mathbf{Z}^{(k)}\,;\,\gamma,\mathbf{\Gamma}_T\big)$ is also straightforward using the IBD-graph representation [Thompson, 2003, Thompson and Heath, 1999b].

Use of the IBD-graph has other immediate advantages. They are generally slowly varying across the chromosome, relative to modern marker densities, and may be output from the MCMC in compact format, with only the change points and changes specified. Once the IBD graph is realized, the pedigree structure is no longer required in subsequent trait-data analyses, providing greater data confidentiality, and the same set of realized IBD graphs may be used for multiple values of $(\gamma, \mathbf{\Gamma}_T)$ and even multiple different traits observed on the same or different subsets of the individuals [Thompson, 2011]. When reduced to the subset of individuals observed for a trait, components of an IBD-graph $\mathbf{Z}$ are generally small, so that for single-locus models $\mathrm{P}(\mathbf{Y}_T \mid \mathbf{Z}\,;\,\gamma,\mathbf{\Gamma}_T)$ is very easily computed, In fact, computation on the joint graphs at several genome locations is also feasible, leading to methods for genetic analysis under oligogenic models [Su and Thompson, 2012]. Finally, the IBD framework has a key advantage in that it is not dependent on the source of the inferred IBD.

Using population-based methods, IBD may be inferred between any two individuals not known to be related [Brown et al., 2012, Browning and Browning, 2010]. If these individuals are pedigree founders or members of different pedigrees, such population-based IBD may be combined with pedigree-based inferences of IBD to create merged IBD graphs, provided greater power and resolution to trait analyses [Glazner and Thompson, 2012].

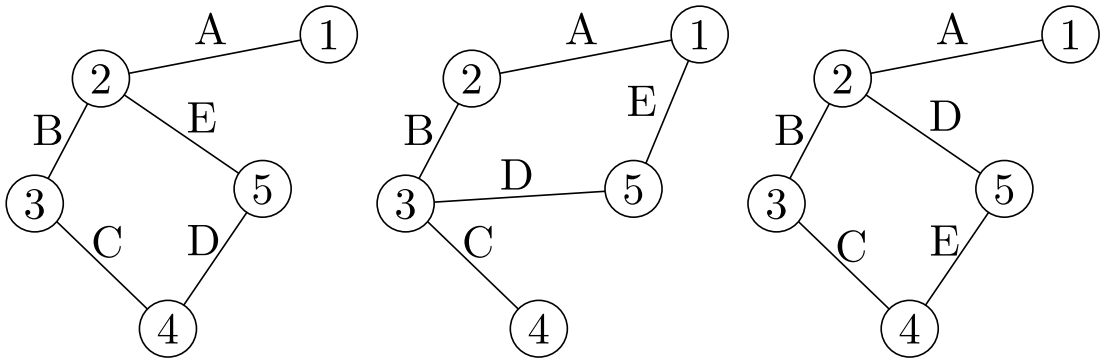
There is another huge computational advantage potentially available from the IBD-graph framework. In an IBD graph, nodes have an identity only through the edges that connect them. Many different inheritance patterns S give rise to the same node-unlabelled IBD graph on the subset of trait-observed individuals. In an MCMC analysis, many different realizations of $\mathbf{Z}$ from $\mathrm{P}(\mathbf{Z} \mid \mathbf{Y}_M\,;\boldsymbol{\Gamma}_M)$ may give the same IBD graph. Additionally, because IBD-graphs are generally slowly varying, a given realized IBD-graph may remain constant over several Mbp. Clearly, $\mathrm{P}(\mathbf{Y}_T \mid \mathbf{Z}\,;\gamma,\boldsymbol{\Gamma}_T)$ should be computed once only for each distinct $\mathbf{Z}$. Recognition of when IBD-graphs are equal and of the marker ranges over which they are equal, is crucial to efficient trait-data analyses. The software developed in this paper performs this task efficiently, and can decrease the burden of the trait-data probability portion of the LOD score estimation procedure by up to two orders of magnitude in real studies [Marchani and Wijsman, 2011].

The key of our approach is to represent the object properties relevant to the testing by sets of representative hashes instead of the objects themselves. Hashes permit much faster algorithms in many cases; for example, testing whether two graphs are equal can be done by checking whether two hashes are equal. These hashes are strong in the sense that intersections – unequal objects or processes mapping to identical hashes – are so unlikely as to never occur in practice. Furthermore, we introduce several provably strong operations on such hashes that allow accurate reductions of collections while maintaining specified relationships between the hashes. Thus in our approach, designing test functions is equivalent to designing composite hash functions accepting one or more input objects and returning a representative hash. Testing equality over collections of input objects is then equivalent to testing equality of the output hashes; set operations over object collections is equivalent to set operations over the hashes, and so on.

We allow the objects in our framework to change over an indexing parameter. We refer to this index as a *marker*, as it refers to genetic marker position in our target application, but it could just as easily refer to time or any other indexing parameter. The power of this framework is that the building block operations process along all the possible marker values; the difficulties introduced by dynamic data is abstracted away.

The running example we use to illustrate this framework are identity-by-descent graphs, or *IBD graphs* [Sobel and Lange, 1996, Thompson and Heath, 1999a]. As an abstracted structure, these graphs have two interesting and distinctive properties. First, only the links are identifiable. In other words, equality on the graph structure is done strictly over links and the set of links attached to each node. Second, these graphs change over marker index; one or more links may be in different configurations between distinct marker points. These graphs can be arbitrarily large, with an arbitrarily large range of marker values over which links can change location, so brute force equality testing at specific marker values quickly becomes infeasible. The computational problems are exacerbated when one wishes to work over large collections of these, matching graph structures and looking for patterns.

To set up this example, consider the graph shown in Figure 1. Snapshots of the graph G are shown at three marker values, $m_1 < m_2 < m_3$. Now consider $G(m_1)$ in Figure 1a. As the nodes and links all have distinct labels, it can be represented by either listing the edges connected to each node or the nodes connected to each edge as shown in Tables 1a and 1b respectively. Note that the structure of the graphs is uniquely described by the sets in the right hand column of either table. This allows us to test a graph structure without considering labels on the nodes but only on the edges, as we do for IBD graphs. For equality testing purposes, this graph can be represented exactly by first computing



(a) $G(m_1)$ (b) $G(m_2)$ (c) $G(m_3)$

Figure 1: An example IBD graph $G[m]$ with labels on both edges and nodes. The nodes (numbered) represent genetic sequences, while the edges (lettered) represent individuals. The graph changes slightly by marker value and is shown at marker values m_1, m_2, and m_3. Note that under the identifiability constraints for IBD graphs, (a) and (c) are distinct despite having the same skeletal structure.

a hash over each connecting set, then over the set of resulting hashes; this is essentially what we do.

Node	Edges
1	A
2	A, B, E
3	B, C
4	C, D
5	D, E

(a)

Edge	Nodes
A	$1, 2$
B	$2, 3$
C	$3, 4$
D	$4, 5$
E	$2, 5$

(b)

Node	Edges
1	A, $E_{[m_2,m_3)}$
2	A, B, $E_{[-\infty,m_2)}$, $D_{[m_3,\infty)}$
3	B, C, $D_{[m_2,m_3)}$
4	C, $D_{[-\infty,m_2)}$, $E_{[m_3,\infty)}$
5	D E

(c)

Table 1: (a, b) Two representations of the graph $G(m_1)$ from Figure 1a, by node (a) and by edge (b). (c) The same graph G at all marker positions with validity sets representing the differences in the graph at marker values $m_1 < m_2 < m_3$.

To extend this to dynamic graphs, we can associate validity information with the components of the graphs. Figure 1 shows G at marker locations $m_1 < m_2 < m_3$, with slight but significant changes between them. Restricting ourselves to looking only at the by-nodes representation in Table 1a, as the other is analogous and this one is appropriate for IBD graphs, we can describe G by Table 1c. This produces a collection of sets that varies by marker value; this example will be explored further throughout this paper since working with dynamic collections such as this one is the target application of our framework.

The paper is structured as follows. In the next section we briefly describe some related work, mostly involving innovative uses of non-intersecting hashes. In section 3, we formalize what we mean by a hash and describe a set of basic functions over them with theoretic guarantees. Then, in section 4, we extend our theory of hashes to include marked hashes by describing marker validity sets and the data structures we use to make marker operations efficient. Section 5 details M-Sets, our most significant contribution, along with available operations. Finally, in section 6, we illustrate the flexibility of our approach with several examples.

2 Related Work

Hash functions and related algorithms have seen numerous applications. The unifying principle is that a short "digest" is calculated over the message or data in such a way that changes in the data are reflected, with sufficiently high probability, in the digest.

Arguably the most widespread use of hash-like algorithms are with check-sums and cyclic redundancy checks (CRCs) [Maxino and Koopman, 2009, Nakassis, 1988, Peterson and Brown]. These are used to verify data integrity in everything from file systems to Internet transmission protocols, and are usually 32 or 64 bit and designed to detect random errors. The checksum is stored or transmitted along with the data. When the data is read or received, the checksum is recalculated; if it doesn't match up with the original checksum, it is assumed that an error occurred.

In cryptography, hashes, or "message digests", give a signature of a message without revealing any information about the message itself [Schneier, 2007]. For example, it is common to store passwords in terms of a hash; it is impossible to deduce what the password is from the hash, but easy to check for a password match. Much like a checksum, it is also used to ensure messages have not been tampered with; as it is extremely difficult to produce different messages that have the same digest. It is this property that we utilize in our approach.

Representing data by a hash is also common. Hash tables, a data structure for fast lookup of objects given a key, works by first creating a hash of the key and using that hash to index a location in an array in which to store the object [Cormen et al., 2001]. The hashes used in such tables are usually weak, as calculating the hash is a significant efficiency bottleneck and the size of the lookup array determines how many bits of the hash are actually needed – usually not all. Collisions – distinct operations mapping to the same hash – may be common, so further equality testing is performed to ensure the indexing keys match. Thus such hash tables tend to be relatively complicated structures.

Stronger hash functions usually produce hashes with 128 or more bits, large enough that the probability of collisions is so low as to never occur in practice. Database applications often use such hashes to index large files, as the non-existence of collisions greatly simplifies processing [Silberschatz et al., 1997]. Similarly, network applications often use such hashes to cache files – files having the same hash do not need to be retransmitted [Barish and Obraczke, 2000, Karger et al., 1999, Wang, 1999]. Often cryptographic hash functions are used for this purpose; while slower, they are computed without using network resources, so calculating them is not the main efficiency bottleneck. Furthermore, they are strong enough that hash equality essentially guarantees object equality.

Our application extends several of these ideas, most notably the last one. We use strong hash functions to represent arbitrary objects in our framework, assuming equalities among hashes are trustworthy. However, our framework extends previous work in that it relies heavily on several operations over hash values to reduce the information present in collections down to a single hash that is invariant to specified aspects of a process. We present several theorems that guarantee the summary hash is also strong. This allows us to reduce computations that would be complex when performed over the original data structures to simple operations over hashes while ensuring that the results are accurate.

3 Hashes

For our purpose, the hash function HASH maps from an arbitrary object or other hash to an integer in the set $\mathcal{H}_N = \{0, 1, ..., N-1\}$ in a way that satisfies several properties. First, such a function must be *one-way*; i.e. no information about the original object can be readily deduced from the hash (e.g. "abcdef" and "Abcdef" map to unrelated hashes). In other words, having access to the output of

such a hash function is equivalent to having access only to an *oracle* function that returns true if a query object is equal to the original and object and, with high probability, false otherwise [Canetti, 1997, Canetti et al., 1998].

Under these requirements, HASH can be seen as a discrete, uniformly distributed random variable mapping from the event space – arbitrary objects or other hashes, etc. – to $\mathcal{H}_N$. This form allows us to assume HASH(ω) has a uniform distribution on $\mathcal{H}_N$ for an arbitrary object ω, a form useful for the proofs we give later on. Furthermore, the "oracle" property implies that the distributions of two hashes are independent if the indexing objects are distinct.

Second, HASH must be strong, i.e. collisions – unequal objects mapping to the same hash – are extremely improbable. Formally,

Definition 3.1 (Strong Hash Function.)**.** A hash function HASH mapping from an arbitrary object ω to a an integer in $\mathcal{H}_N = \{0, 1, ..., N-1\}$ is considered *strong* if, for $h_1 = \text{HASH}(\omega_1)$ and $h_2 = \text{HASH}(\omega_2)$,

$$\mathrm{P}(h_1 = h_2) = \begin{cases} 1 & \omega_1 = \omega_2 \\ 1/N & \omega_1 \neq \omega_2 \end{cases} \tag{2}$$

The idea is to set N large enough (in our case around 10^{38}) that the probability of two unequal objects yielding the same hash is so low as to never occur in practice. However, in light of the fact that collisions can theoretically occur with nonzero probability, we denote inequality as $\nsim$ instead of $\neq$; specifically, if $h_1 = \text{HASH}(\omega_1) \nsim \text{HASH}(\omega_2) = h_2$, then $\mathrm{P}(h_1 = h_2) = 1/N$.

We may assume the existence of such a hash function, denoted here as HASH, which maps any possible input – strings, numbers, other hashes – to a hash that satisfies definition 3.1. This assumption is reasonable, as significant research in cryptography has gone towards developing hash functions that not only satisfy definition 3.1, but also prevent adversaries with large amounts of computing power against deducing any information about the original object [Goldreich, 2001, Schneier, 2007]. These hash functions are widely available and have open specifications; we use a tweaked version of the well known MD5 hash function as outlined in appendix Appendix A.

3.1 Hash Operations

Based on the existence of a hash function HASH, and simple operations on integers in $\mathcal{H}_N$, we propose two basic operations to combine and modify hashes. The first is a way to summarize an unordered collection of hashes by reducing it to a single hash that is sensitive to changes in the hash value of any key in the original collection. The second, to be used in nested function compositions, is a way to scramble a reduced hash value so that it locks invariance properties present earlier in the function composition. In this section, we formally describe these operations, which will later be generalized to both marked hashes and then to collections of marked hashes.

3.1.1 Transformations

We now must formalize what we mean by a transformation in the testing function context. In our terminology, a transformation always applies to the inputs of a testing function and is done without regard to the hash values themselves. For example, any reordering of the input values is a valid transformation, but appending a precomputed string to the label of an input object to cause its hash to be the special null-hash – all zeros – is not (Note, however, that forming the null-hash in this way is near-impossible in practice). Formally,

Definition 3.2 (Transformation Classes)**.** A transformation class for a testing function $\mathcal{T}$ satisfies:

T1. Every $T \in \mathcal{T}$ can be expressed as a transformation of the non-hash input objects.

T2. No $T \in \mathcal{T}$ takes account of the specific hash values produced by these objects.

Given these restrictions on transformation classes, we can now formally define what we mean by invariance.

Definition 3.3 (Invariance and Distinguishing)**.** A function $f : \mathcal{H}_N^n \mapsto \mathcal{H}_n$ accepting a set of inputs $\mathbf{h} = (h_1, h_2, ..., h_n)$ is *invariant* under a class of transformations $\mathcal{T}$ if $f(T\mathbf{h}) = f(\mathbf{h})$ for all $T \in \mathcal{T}$ and for all $\mathbf{h} \in \mathcal{H}_N$. Likewise, f *distinguishes* $\mathcal{T}$ if, for $T_1, T_2 \in \mathcal{T}$, $f(T_1\mathbf{h}) \nsim f(T_2\mathbf{h}) \nsim f(\mathbf{h})$ unless $T_1\mathbf{h} = \mathbf{h}$, $T_2\mathbf{h} = \mathbf{h}$ or $T_1\mathbf{h} = T_2\mathbf{h}$.

In other words, the output hashes change under distinguishing transformations and are constant under invariant transformations. With these formal definitions, we are now prepared to define atomic operations that have specific and provable invariance properties.

3.1.2 The Null Hash

We chose one value in our hash set, specifically 0, to represent a *Null* hash. This hash value, denoted as $\emptyset$, is used to represent the absence of an input object. It most commonly represents the hash of an object that is outside its marker validity set; this will be detailed more in section 4. As such, it has special properties with the hash operations outlined in the next section.

3.2 Hash Operation Properties

We here propose two basic operations, REDUCE and REHASH. The first reduces a collection of n hashes, $h_1, h_2, ..., h_n$ for $n = 1, 2, ...$, down to a single hash, while the second rehashes a single input hash to prevent invariance properties from propagating further through a function composition. The key aspects of these operations are what transformations over the inputs they are invariant under; we describe these next. We follow this with a brief discussion of the implications of these results, before detailing the construction of such functions in section 3.3.

Definition 3.4 (REDUCE)**.** For the REDUCE function, with $h_0 = \text{REDUCE}(h_1, ..., h_n)$, we have the following properties:

RD1. *Invariance Under the null hash* $\emptyset$. The output hash h_0 is invariant under input of the null hash $\emptyset$. Specifically,

$$\text{REDUCE}(h_1, \emptyset) = \text{REDUCE}(h_1)$$
$$\text{REDUCE}(\emptyset) = \emptyset$$

RD2. *Invariance Under Single Mapping.* The output hash h_0 equals the input hash h_1 if $n = 1$. Specifically,

$$\text{REDUCE}(h_1) = h_1$$

RD3. *Existence of a negating hash.* There exists a negating hash, here labeled $-h_1$, that cancels the effect of an input hash in the sense that

$$\text{REDUCE}(h_1, -h_1) = \text{REDUCE}(\emptyset) = \emptyset$$

RD4. *Order Invariance.* The output hash h_0 is invariant under different orderings of the input. Specifically,

$$\textsc{Reduce}(h_1, h_2) = \textsc{Reduce}(h_2, h_1).$$

RD5. *Invariance Under Composition.*The output hash h_0 is invariant under nested compositions of Reduce. Specifically,

$$\begin{aligned}\textsc{Reduce}(h_1, h_2, h_3) &= \textsc{Reduce}(h_1, \textsc{Reduce}(h_2, h_3)) \\ &= \textsc{Reduce}(\textsc{Reduce}(h_1, h_2), h_3)\end{aligned}$$

RD6. *Strength.* The Reduce function distinguishes all other transformations in the sense of definition 3.3 (e.g. an input value is dropped or changed).

Two remarks are in order. First, property RD5 allows us to expand all nestings of Reduce to a single function of hashes that are not the output of Reduce operations. For example,

$$\textsc{Reduce}(h_1, \textsc{Reduce}(h_2, \textsc{Reduce}(h_3, h_4))) = \textsc{Reduce}(h_1, h_2, h_3, h_4)$$

The implication is that when we have a collection of input hashes $h_1, h_2, ..., h_n$, which may or may not have come from a reduction themselves, we can write their reduction out as a single reduction; i.e.

$$\textsc{Reduce}(h_1, h_2, ..., h_n) = \textsc{Reduce}(h'_1, h'_2, ..., h'_{n'})$$

for some hashes $h'_1, h'_2, ..., h'_{n'}$ that are not the result of Reduce.

Second, property RD3 allows us to remove elements from a reduction once they are added, making the reduced hash invariant under changes in whatever process produced the canceled hash. This property becomes especially useful later on when working with intervals; the output hash varies as a function of a marker value, and a hash h valid on an interval $[a, b)$ of that marker can be added once at a and removed at b, with the net result being that the output hash is only sensitive to h on $[a, b)$.

Definition 3.5 (Rehash)**.** For the Rehash function, we have only two properties, which we list here.

RH1. *Invariance Under the null hash* $\emptyset$.The output hash h_0 is invariant under input of the null hash $\emptyset$. Specifically,

$$\textsc{Rehash}(\emptyset) = \emptyset$$

RH2. *Strength.* The Rehash function is strong in the sense of definition 3.1, in which the object space is restricted to hash keys.

The purpose of the Rehash function is to freeze invariance patterns from propagating through multiple compositions. Returning to the example IBD graph in Figure 1, consider the testing function shown in Figure 2. The function resulting from chaining Reduce and Rehash together as shown is invariant under changes in the node labels or orderings of the edges within each node, but is sensitive to any structural change in the graph. This can be proved by decomposing the nested Reduce functions into a single function of the first group; all the invariant relationships of this single function are present in the original. However, the final reduce cannot be decomposed this way on account of the Rehash functions.

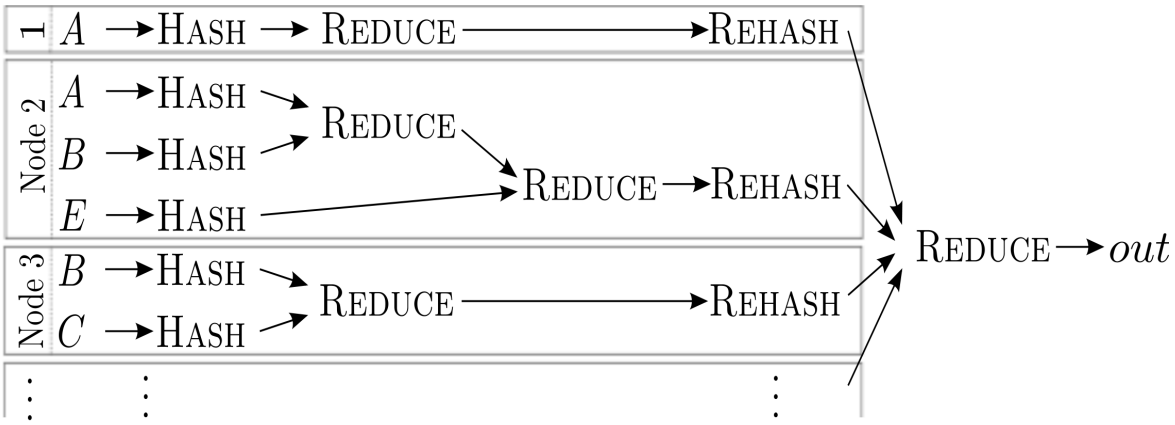


Figure 2: Part of a composite function for testing equality, ignoring node labels, of the graph $G(m_1)$ in Figure 1. The part of the function for the first 3 nodes are shown. For each node, the labels on the connected edges are reduced into one hash, and then the hashes representing the nodes are reduced to a final hash which represents the graph. This final hash is invariant under changes in the node labels or orderings of the edges within each node, but is sensitive to any structural change in the graph.

3.3 Function Construction and Implementation

We now establish that functions Reduce and Rehash satisfying the appropriate properties exist. Along with this comes a requirement on N, namely that it is *prime*; this is required to preserve the strength of the Reduce function under multiple reductions of the same hash key.

3.3.1 Basic Operations

Before presenting the Reduce and Rehash functions, we first present two lemmas from elementary number theory. These lemmas provide the theoretical basis of the Reduce function.

Lemma 3.6. *Let N be prime, and let $\oplus$ and $\otimes$ denote addition and multiplication modulo N, respectively. Suppose $a, b \in \mathcal{H}_N$. Then the following equivalences hold modulo N:*

$$\begin{aligned} (a \otimes b) \oplus b &\equiv (a \oplus 1) \otimes b \\ -(a \oplus b) &\equiv (-a \oplus -b) \\ -(a \otimes b) &\equiv (-a \otimes b) \equiv (a \otimes -b) \end{aligned} \tag{3}$$

Proof. The integers modulo N forms an algebraic field with distributivity of multiplication over addition, so ((3)) is trivially satisfied. Furthermore,

$$-h \equiv (-1) \otimes h \equiv (N-1) \otimes h \mod N$$

Thus $-(a \oplus b) \mod N \equiv (-a \oplus -b) \mod N$. Similarly, multiplication is commutative, so

$$\begin{aligned} -(a \otimes b) &\equiv ((-1) \otimes a) \otimes b \equiv (-a \otimes b) \mod N \\ &\equiv (a \otimes ((-1) \otimes b)) \equiv (a \otimes -b) \mod N \end{aligned}$$

The lemma is proved. □

Lemma 3.7. *Let N be prime, and let X and Y be independent random variables with distribution $\mathcal{U}n(\mathcal{H}_N)$, i.e. uniform over $\mathcal{H}_N$, and let r be any number in $\mathcal{H}_N$. Then*

$$C \oplus X \sim \mathcal{U}n(\mathcal{H}_N) \tag{4}$$
$$-X \mod N \equiv N - X \sim \mathcal{U}n(\mathcal{H}_N) \tag{5}$$
$$X \oplus Y \sim \mathcal{U}n(\mathcal{H}_N) \tag{6}$$
$$r \otimes X \sim \mathcal{U}n(\mathcal{H}_N), \tag{7}$$

i.e. the above are all uniformly distributed on $\mathcal{H}_N$.

Proof. For (4), note that addition modulo a constant is a one-to-one automorphic map on the hash space, thus every mapped number is equally likely. (5) is similarly proved. To prove (6), note that Y can be seen as a similar random mapping; however, every possible mapping produces the same distribution over $\mathcal{H}_N$, so $X \oplus Y$ has the same distribution as $X \oplus Y \mid Y$, which, by (4) is uniform on $\mathcal{H}_N$.

For (7), recall from number theory that r has an inverse $\mod N$ if and only if r and n are coprime, i.e. $\gcd(r, n) = 1$. Thus if N is prime, each r in $\mathcal{H}_N$ also indexes a one-to-one automorphic map under $r \otimes X$, and the result immediately follows. □

3.3.2 Reduce

We are now ready to tackle REDUCE; if N is prime, then addition modulo N satisfies all the required properties. This operation is similar to part of the Fletcher checksum algorithm, which uses addition modulo a 16-bit prime for the reasons outlined in lemma 3.7.

Theorem 3.8 (The REDUCE Function.)**.** *Suppose N is prime. Then the function $f : \mathcal{H}_N^n \mapsto \mathcal{H}_N$ defined by*

$$\begin{aligned} f(h_1, h_2, ..., h_n) &= h_1 + h_2 + ... + h_n \mod N \\ &= h_1 \oplus h_2 \oplus ... \oplus h_n, \end{aligned}$$

where $\oplus$ denotes addition modulo N, satisfies properties RD1-RD6.

Proof. Addition modulo N, with N prime, forms an algebraic group, so properties RD1, RD2, RD4 and RD5 are trivially satisfied. RD3 is satisfied with $-h_1 \equiv N - h_1 \mod N$.

To prove RD6, it is sufficient to verify equation (2) in definition (T1). Let $h_0 = \text{REDUCE}(h_1, h_2, ..., h_n)$, and let $k_0 = \text{REDUCE}(k_1, k_2, ..., k_m)$. Without loss of generality, by the previous properties, let the sequences be as follows:

1. No hash in either sequence is the negative of another hash in that sequence.
2. $n \geq m$; if not, swap sequences.
3. There exists an index $q \in \{1, 2, ..., m\}$ such that $h_i = k_i$ for $i \leq q$ and $h_i \notin \{k_{q+1}, ..., k_m\}$ for $i = q + 1, ..., m$.
4. $h_1 = k_1 = \emptyset$ (so $q \geq 1$, to make bookkeeping easier).

Now suppose the two sequences are identical, so $n = m = q$. Then $h_0 = k_0$ and we are done; this satisfies the first part of equation (2). Otherwise, we can use lemma 3.6 to represent h_0 and k_0 as

$$\begin{aligned} h_0 &= Q \oplus (\alpha_1 \otimes H_1) \oplus (\alpha_2 \otimes H_2) \oplus \cdots \oplus (\alpha_{n'} \otimes H_{n'}) \\ k_0 &= Q \oplus (\beta_1 \otimes K_1) \oplus (\beta_2 \otimes K_2) \oplus \cdots \oplus (\beta_{m'} \otimes K_{m'}) \end{aligned}$$

where $Q = \textsc{Reduce}(h_1, h_2, ..., h_q)$ and $H_1, H_2, ..., H_{n'}, K_1, K_2, ..., K_{m'}$ are all independent and $\alpha_1, ..., \alpha_{n'}, \beta_1, ..., \beta_{m'}$ denote the multiplicity of each hash. Now it remains to show that $\mathrm{P}(h_0 \equiv k_0 \mod N) = 1/N$. Now

$$\mathrm{P}(h_0 \equiv k_0 \mod N) = \mathrm{P}(h_0 \oplus -k_0 \equiv 0)$$

and, using lemma 3.6 to distribute the minus signs and eliminate the Qs,

$$\begin{aligned} h_0 \oplus -k_0 = (\alpha_1 \otimes H_1) \oplus (\alpha_2 \otimes H_2) \oplus \cdots \oplus (\alpha_{n'} \otimes H_{n'}) \\ \oplus (\beta_1 \otimes -K_1) \oplus (\beta_2 \otimes -K_2) \oplus \cdots \oplus (\beta_{m'} \otimes -K_{m'}). \end{aligned}$$

However, applying lemma 3.7 inductively gives that the distribution of the above is uniform over $\mathcal{H}_N$. Thus $\mathrm{P}(h_0 = k_0) = 1/N$. □

3.3.3 Rehash

Now on to Rehash, which is far simpler as it relies mainly on the property of the hash function being strong. The only extra work is to ensure that the null hash is preserved.

Theorem 3.9 (Rehash)**.** *The function* $\textsc{Rehash} : \mathcal{H}_N \mapsto \mathcal{H}_N$ *defined by*

$$\textsc{Rehash}(h) = \textsc{Reduce}(\textsc{Hash}(h), -\textsc{Hash}(\emptyset)),$$

satisfies properties (RH1)-(RH2) while distinguishing all other transformations.

Proof. Follows trivially from the properties of Reduce and the assumption that Hash is strong and one-way. □

In this section, we have presented the fundamental building blocks regarding hashes. We now augment these hash values with validity information that varies as a function of a particular parameter, here called a marker value.

4 Hashes and Keys

We define a *key* as a hash value associated with a set of intervals within which that hash, or the object it refers to, is valid. A key may represent an object in the data structure we wish to design a testing function for, e.g. an edge in a graph that is present only for certain marker values, or it may represent the result of a process or sub-process. At the marker values for which this key is not valid, we assume its hash is equal to $\emptyset$. To denote the hash value of any key at a certain value p of the parameter space, we use brackets – e.g. $h[p]$.

The set on which the hash value of a key is valid, which we call a *marker validity set* or just *validity set*, is a sequence of sorted, disjoint intervals of the form $[a_i, b_i) \subseteq [-\infty, \infty)$. A *marked* object is *valid* in each of these intervals and *invalid* elsewhere. Saying something is *unmarked* is equivalent – for bookkeeping reasons – to saying that it is always valid, i.e. on the interval $[-\infty, \infty)$.

5 Marked Sets

The M-Set, a container of marked keys, is the most powerful component of our framework. It can be thought of as a collection of marked objects, stored as representative keys, that permits easy access to useful information about the collection. The idea is that one can express many algorithmically

complicated processing tasks involving dynamic data as simple operations on and between M-Set objects. Efficient operations on an M-Set include querying, insertion, deletion, testing collection equality at specific marker values or over the whole collection, union and intersection, and extracting the collection of keys valid at specific marker values.

5.1 Operations

Available M-Set operations fall into five categories: *element operations* like insertion, querying, or modifying an element's validity set; *hash and testing operations* like determining whether two M-Sets are identical at marker m; *set operations* such as union and intersection; *validity set operations* such as extracting all hashes valid at a certain point; and *summarizing operations* which produce representative hashes from one or more M-Sets. Of these, operations in the first four categories are easily explained; we present them in the next sections. The summarizing operation, which is key to the power of our framework, is presented in section 5.2. A list of all these functions is given in section B.2; the most powerful ones we describe now.

5.2 Summarizing Operations: ReduceMSetand Summarize

The natural generalization of Reduce to M-Set objects, ReduceMSet, returns an M-Set containing the reduction of every key in the set. Formally, for M-Sets T_0 and T_1, suppose $T_0 = \text{ReduceMSet}(T_1)$. Then, for each marker value m, there is exactly one key in T_0 valid at m, with that hash being the Reduce of every key in T_1 valid at m. The M-Set is the appropriate output of this function, as the resulting hash value varies arbitrarily by marker value and thus cannot be expressed as a single key. Because such an M-Set has exactly one hash (possibly $\emptyset$) valid at each marker value, we use the same bracket notation as keys to refer to that hash value, e.g. $T[m]$.

Looking up the reduced hash of the M-Set at specific marker locations – HashAtMarker – is efficient to do without reducing the entire set. The main use for ReduceMSet is thus to create a lookup of the possible values of Reduce in that set and when they are valid as represented by the validity sets of the resulting keys. This can, for example, be used to determine the set on which a dynamic collection is equal to a given collection.

Just as ReduceMSet summarizes the information in a collection of keys by a single M-Set, so Summarize reduces the information from one or more distinct collections of M-Sets down to a single M-Set over which computations can accurately and efficiently be done. Changes in any individual collection, as well as which collections are included, are always reflected in the summarizing M-Set unless they fall under one of the invariant properties (e.g. $\emptyset$ does not affect the outcome).

As such, Summarize produces an M-Set T in which one hash is valid at each given marker position m. For $T = \text{Summarize}(T_1, T_2, ..., T_n)$, the hash key valid at m, $T[m]$, is equal to

$$T[m] = \text{Reduce}(\{\text{Rehash}(h) \ : \\ h = \text{ReduceMSet}(T_i) \text{ at } m, \text{ for } i = 1, 2, ..., n\})$$

Given our implementation of ReduceMSet, described in the next section, the Summarize operation is very efficient and a central building-block in our framework.

The summarizing operation is useful in that it allows us to efficiently test equality of collections of M-Sets using the operations designed for hashes. For example, suppose we have two summary M-Sets, $T = \text{Summarize}(T_1, T_2, ..., T_n)$ and $U = \text{Summarize}(U_1, U_2, ..., U_n)$. Given $T[p]$, the marker validity set of the corresponding key in U, if any, gives the set in which the collection of T_i's at p is equal to the collection of U_i's. Likewise, MarkerUnion over all objects in the intersection of T and U gives the locations at which the two collections are equal.

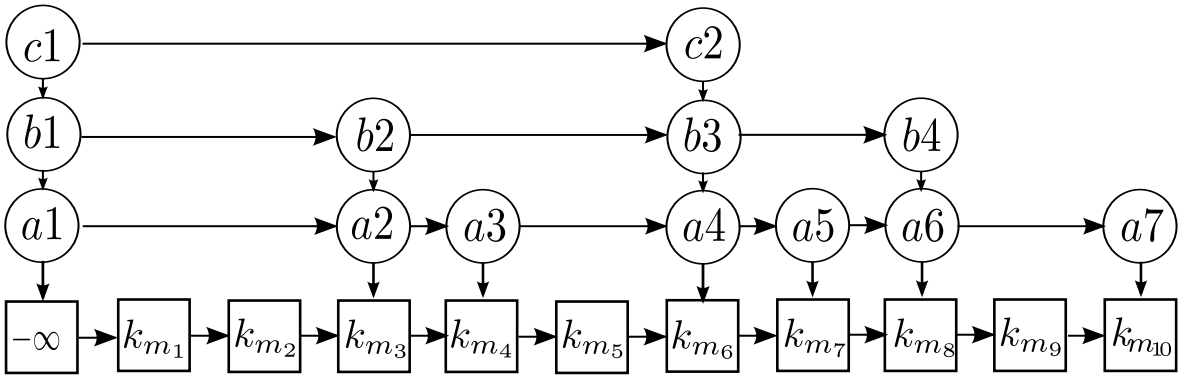


Figure 3: A skip-list with 3 levels and 10 values.

5.3 Implementation

Internally, an M-Set is a combination of a hash table to store the hashes and a skip-list-type structure that handles the bookkeeping operations dealing with validity sets. This latter structure efficiently tracks the REDUCE at each marker value of all keys present in the structure; this is key to making operations like equality testing and summarizing efficient.

5.3.1 Skip Lists for Markers

To introduce the augmented skip-list for the REDUCE lookup, we first describe a simpler version for holding marker information. In a skip-list, the values are stored in a single ordered linked list; this allows for easy insertion and deletion, but by itself does not permit efficient access. To access them efficiently, there are additional levels of increasingly sparse linked lists, each a subset of the previous, with each node pointing forward and pointing down to the corresponding node in the lower level. When a new value is inserted in the skip-list – in our case a validity interval – it also adds corresponding nodes in the L levels above it, where $L \sim \mathit{Geometric}(p)$. The geometric distribution of the node "heights" means the expected size of level L is np^L. Overall, the expected times for querying, insertion, or deletion is $\mathcal{O}(\log n)$ [Devroye, 1992, Kirschenhofer and Prodinger, 1994, Papadakis et al., 1992].

An example skip-list is shown in Figure 3. In this skip-list, each marker location, denoted by $k_{m_1}, ..., k_{m_n}$, has corresponding nodes in 0 to 3 levels above it. The interval starting values are stored in the nodes at each level.

Querying is done as follows. Start at the first node in the highest level, which is always at $-\infty$. If a forward node exists and its value is less than or equal to the query value, move forward; otherwise, move down. Repeat this until you're on the lower level and cannot advance any farther; if this interval contains the query value, that marker value is valid, otherwise it is not. Finding locations for insertion and deletion are analogous.

5.3.2 Internal Reduce Lookup

We now present the data structure that comprises the second component of an M-Set. This structure allows for calculating REDUCE, for a given marker value, over all components of the entire hash collection in logarithmic time while still allowing logarithmic time insertion and deletion. With this

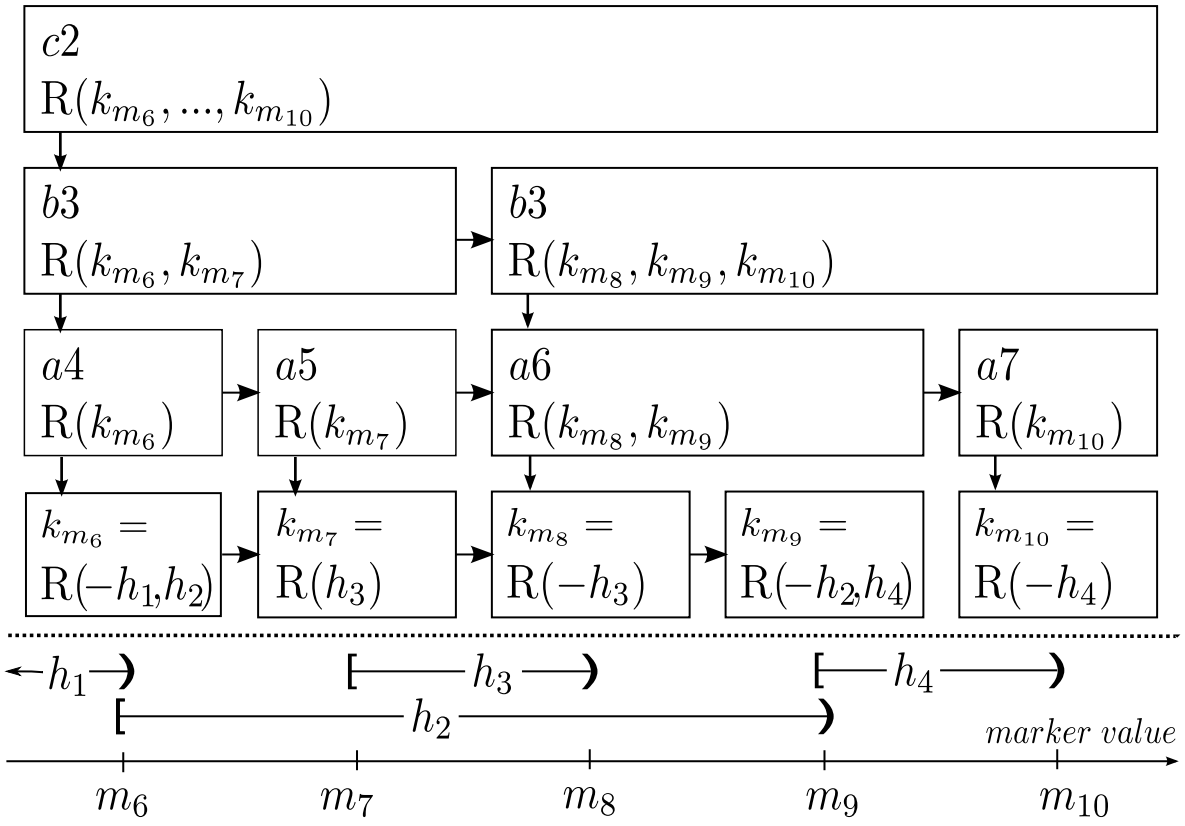


Figure 4: The left part of the table in Figure 3 adapted to be an M-Set hash lookup structure holding hash information in the skip-list nodes. Hash keys, valid for certain marker intervals, are shown in the bottom, while the information stored in each node is shown below the node label.

structure, we can also calculate REDUCE over all validity set intervals values in time linear in the number of distinct validity interval endpoints, producing a new M-Set of keys with non-intersecting validity sets representing the different values of REDUCE at various marker intervals. These algorithmic bounds and the associated algorithms will be formalized below.

The structure we propose is an augmented skip-list. The leaf and node values present in the tree correspond to the interval endpoints in the validity intervals of any key present, i.e. the marker values where the validity of any key changes. This list is augmented to hold a hash key in each leaf and each node.

The main idea for the leaf hashes is to track REDUCE over all valid keys as a function of marker value m. Stepping through the leaves, starting with the hash value in the first leaf and updating it with the leaf hash using REDUCE, yields REDUCE over all valid hashes at each marker value. This is done by including a hash at the beginning of each of its validity interval and the negative of that hash at the end of a validity interval. Thus hash values are added and removed from the overall reduced hash to maintain the value of REDUCE at each marker value. This allows us, additionally, to calculate the M-Set produced by REDUCEMSET efficiently by simply stepping through the leaves.

Figure 4 shows an example augmented skip-list, the structure of which is taken from the right half

of the example skip-list in Figure 3. The leaves hold hash values that are the reduction of hash values and/or negative hash values. At a given marker value, the value of REDUCE over all previous leaves is the value of REDUCE over all currently valid keys. For example, looking at the first three leaves,

$$\begin{aligned}
&\textsc{Reduce}(k_{m_6}, k_{m_7}, k_{m_8}) \\
&\quad = \textsc{Reduce}(\textsc{Reduce}(h_1, h_2), \textsc{Reduce}(-h_1, h_3), \textsc{Reduce}(-h_3)) \\
&\quad = \textsc{Reduce}(h_1, h_2, -h_1, h_3, -h_3) \\
&\quad = \textsc{Reduce}(h_2)
\end{aligned}$$

Formally, we maintain the following property:

Property 5.1 (M-Set Marker Skip-List Leaf Hashes)**.** *For a given M-Set T with skip-list S, let*

$$\begin{aligned}
L[m] &= \{h : m = \ell \text{ for some } [\ell, u) \text{ in the validity set of } h\} \\
U[m] &= \{h : m = u \text{ for some } [\ell, u) \text{ in the validity set of } h\}
\end{aligned}$$

Then for all leaves in S, define the hash value $r_0[m]$ at that leaf to be

$$r_0[m] = \textsc{Reduce}(\{h : h \in L[m]\} \cup \{-h : h \in U[m]\})$$

Thus we can formally state the above.

Theorem 5.2. *Let T be an M-Set with corresponding leaf nodes $r_0[\cdot]$. Let $R[m] = \textsc{Reduce}(\{r_0[m'] : m' \leq m\})$. Then*

$$R[m] = \textsc{Reduce}(\{h[m] : h \in T \text{ and } h \text{ is valid at } m\}),$$

Equivalently,

$$R[m] = \textsc{Reduce}(\{h[m] : h \in T\}),$$

Proof. On the marker intervals where a hash key is valid, its hash is included in $R[m]$ exactly one time more than its inverse is included, and it is included exactly the same number of times as its inverse at all other values. From property RD3, the summary REDUCE hash at m depends on a hash key if and only if that hash key it is valid at m. The equivalent formula for $R[m]$ follows immediately from the fact that $h[m] = \emptyset$ if h is not valid at m; which does not change $R[m]$. □

As mentioned, the REDUCE of all leaf hash values whose associated marker value is less than or equal to the given marker value m is equal to the REDUCE of all the keys in the M-Set valid at m. However, storing the hashes in this way at the leaves is not enough to efficiently compute REDUCE quickly over the full hash table at a given marker value m, as it would require visiting every change-point present that is less than m. One might suggest storing $R[m]$, the full value of REDUCE, at the leaves instead of just $r_0[m]$, but then insertion and deletion would require time linear in the number of marker points present in valid intervals, and this can be arbitrarily large.

Our solution is to store a hash value summarizing blocks of $r_0[m]$ in the nodes at higher levels in the skip-list structure. The idea is that the hash value stored in the nodes is the reduction of all leaves under it. The presence of these hash values at the nodes allows us to construct logarithmic time algorithms for querying, insertion and deletion. The idea is that we can include the reduction of large blocks of nodes with a single operation as we travel down the skip-list.

Formally, at the nodes, these hash values maintain the following property:

Algorithm 1: HashAtMarkerValue

Input: M-Set T and marker value m.
Output: Hash Value h, the Reduce over all hash objects in T at m.

$h \leftarrow 0$
$n \leftarrow$ First node of highest level of skip-list of T

while *not at destination leaf* **do**
  if *next node* n' *has marker value* $\leq m$ **then**
    $h \leftarrow \text{Reduce}(h, \text{hash at node } n)$
    $n \leftarrow n'$
  else
    $n \leftarrow$ node below n
return h

Property 5.3 (M-Set Skip-List Node Property)**.** *Let $r_b[m]$ be a hash value at marker value m in the bth level of the skip-list with $b \geq 1$ ($b = 0$ is the leaf level). Let m' be the smallest marker value larger than m, possibly ∞, such that there exists a node at level b with marker value m'. Then*

$$r_b[m] = \text{Reduce}(\{r_{b-1}[m''] : m \leq m'' < m'\}).$$

Equivalently,

$$r_b[m] = \text{Reduce}(\{r_0[m''] : m \leq m' \leq m''\}) \tag{8}$$

In other words, the hash value of a node at level b, $b \geq 1$, with marker value m is the Reduce over all nodes at level $b-1$ whose marker value is greater than m and less than the marker value of the next node at level b. Property RD5 of the reduce function – invariance under composition – means that the hash value stored in a node is the Reduce over all the leaf values beneath it, i.e. reaching such a leaf requires passing through that node. This yields the equivalent formula (8).

In Figure 4, the hash at node $c2$ is the Reduce over the hash at nodes $b3$ and $b4$; the hash at node $b3$ is the Reduce over the hash at nodes $a4$ and $a5$, and so on. The net result of this is that the hash at each node is the Reduce of all the hash values beneath it.

This allows us to calculate Reduce at any marker value in logarithmic time using Algorithm 1. This algorithm differs from the regular skip-list query algorithm only in that it updates a running hash as it traverses sideways. This means that at each point, the current hash h includes the reduction of all leaf nodes prior to the current marker value, i.e. before moving forward, the reduction of all leaf hashes between the current node and the next node is included in Reduce. This last statement is sufficient to prove the validity of the algorithm.

The algorithms for insertion and deletion are similar but involve more detailed bookkeeping to handle the creation and deletion of nodes. Apart from this, the only difference from Algorithm 1 is that the hash at the node is updated when moving down, rather than across; this preserves the invariant that the hash at a given node is the Reduce of all the hash values stored under it.

6 Example

We now return to the motivating example, IBD graphs, given in section 1. The individuals in this case are edges, which are assumed to be unique; the labels on the nodes are unidentifiable, requiring any testing functions to be invariant to them.

Algorithm 2: IBD Graph Summarizing

Input: An IBD Graph G.
Output: T, an M-Set summarizing G; the hash of T at a marker point m is invariant under permutations of the node labels.

$L \leftarrow$ Empty list

for *Each node n in G* **do**
  $T \leftarrow$ Empty M-Set
  for *Each edge e attached to n on interval $[t_1, t_2)$* **do**
    $h \leftarrow \textsc{Hash}(e)$
    `/* Set` $[t_1, t_2)$ `with key` h `to be valid in` T. `*/`
    $\textsc{AddValidRegion}(T, h, t_1, t_2)$
  `/* Append this new M-Set` T `to our list. */`
  append T **to** L
`/* The hash representation of the graph is the summary of all the graphs in` L. `*/`
$T \leftarrow \textsc{Summarize}(L)$
return T

Algorithm 3: IBD Graph Unique Elements

Input: $S_1, S_2, ..., S_n$, M-Sets summarizing n IBD graphs.
Output: L, a list of $(h,\ mi,\ m)$ tuples giving a reference hash, an index, and a marker location denoting one instance of each unique graph in the original collection.

`/* Form a single table of all unique graph hashes. */`
$H \leftarrow \textsc{Union}(\textsc{KeySet}(S_1), \textsc{KeySet}(S_2), ..., \textsc{KeySet}(S_n))$
`/* Go through and find one index and marker value where each of these graphs occur.` H `tracks the graph hashes yet to be recorded. */`
$L \leftarrow$ Empty list
for $i = 1$ **to** n **do**
  $S \leftarrow \textsc{Intersection}(S_i, H)$
  foreach h **in** S **do**
    append $(h, i, \textsc{VSetMin}(h))$ **to** L
    $\textsc{Pop}(H, \textsc{Key}(h))$
return L

The main idea is to represent each node as an M-Set with keys representing edge labels. The validity set on each key denotes when that edge is attached to the node; this allows the structure of the graph to change over marker location. With each node represented this way, the entire graph can represented as the summary of the node M-Sets. At each marker point, this computes a hash over each edge within a node using Reduce, rehashes the result to freeze invariants, then computes a final hash over the resulting collections. Per the guarantees of Reduce and Rehash (definitions 3.4 and 3.5), the resulting hashes of two graphs will match if and only all the nodes have identical edges, which is true if and only if the two graphs are equivalent (ignoring the completely negligible probability of hash intersections).

Our first illustration, given in Algorithm 2, simply tests if two graphs are equal. It also illustrates

how to set up the original graphs from a simple list-of-lists form. Beyond this, we are also be interested in all the unique graphs present in a collection of node M-Sets. Assuming these are summarized by $S_1, S_2, ..., S_n$ as in Algorithm 2, we can use algorithm 3 to find a list of specific indices and marker locations that enumerate the unique graphs. Algorithms that need to be run, in theory, at each marker value can instead be run only at this set of points.

7 Experiments and Benchmarks

To demonstrate the effectiveness of this approach, Table 2 presents computation times on several real and simulated IBD graph collections along with the savings incurred by avoiding redundant operations. The experiments were all run on an Intel Xeon E5-4640 processor running at 2.40 GHz. Recall that the motivating computations to be run on the unique graphs (described in section 1) can hours when run on a collection of these graphs, so even a small reduction factor gives a significant time savings and easily absorbs the preprocessing time shown here. *Total Graph Configurations* is the number of potentially different graphs over which a computation needs to be run. On a single graph, it is the total number of intervals on which there is no recorded change in the graph; for multiple graphs, it is this factor summed over all graphs. *Unique Graphs* is the number of unique configurations within this set; running computations only on each of these is sufficient.

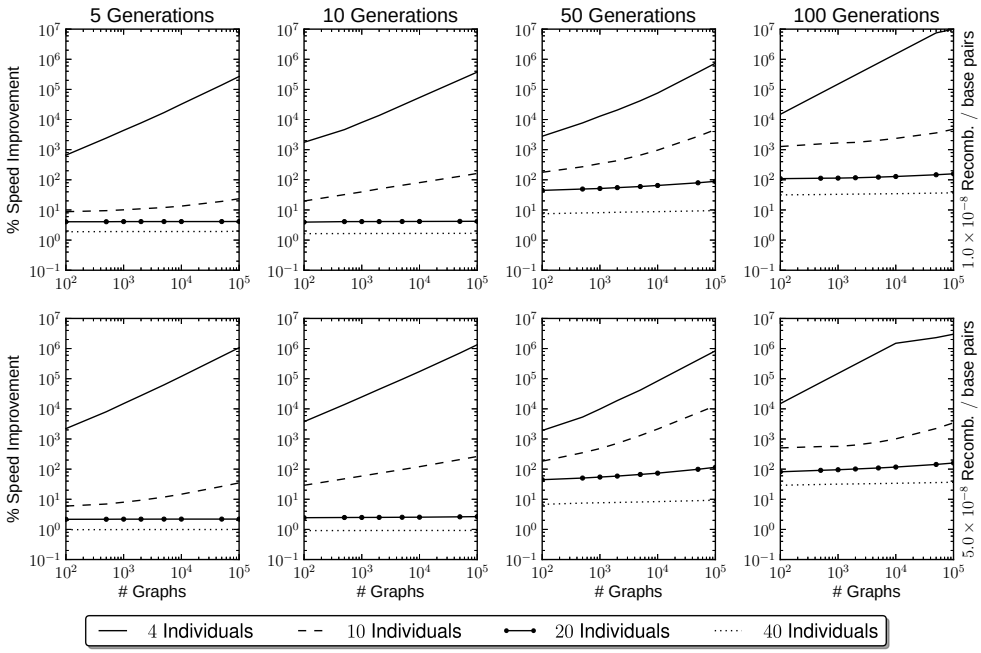
Dataset	**Number of Graphs**	**Individuals per Graph**	**Total Graph Configurations**	**Unique Graphs**	**Speedup Factor**	**Computation Time**
Iceland-1	1000	95	155,612	150,290	1.04	2.18s
Iceland-2	1000	31	67,809	1,179	57.5	0.99s
Iceland-3	30000	31	1,616,028	1,376	1174.4	12.16s
fglhaps-7	1	7000	92,488	92,483	1.00005	10.39s

Table 2: Result and processing times for Algorithm 3 on several IBD graph datasets.

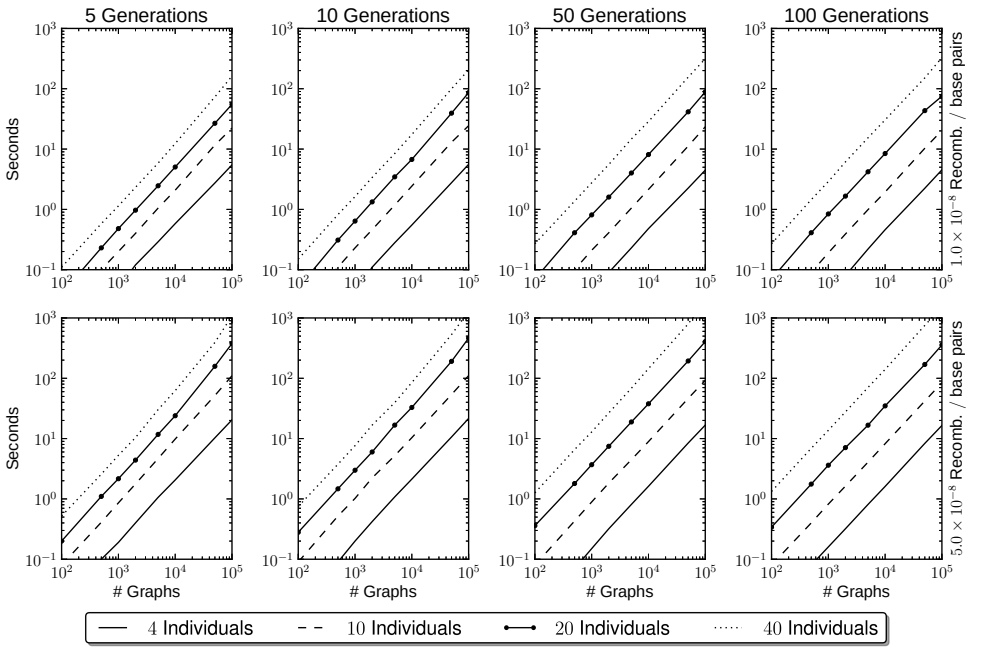
Table 2 shows results for four examples. The three Iceland datasets consist of IBD graphs realized conditionally on marker data. The marker data are simulated on a pedigree structure described in [Glazner and Thompson, 2012]. Iceland-1 IBD graphs contain a full set of 95 related individuals over 12 generations, while the graphs of Iceland-2 and Iceland-3 are of a reduced set of individuals in the last 3 generations for whom marker and trait data were assumed available. The fglhaps-7 example is a single IBD graph with 7000 individuals and marker indexing from 1 to 140 million. This graph results from simulation of descent of a population of 7000 individuals over 200 generations [Brown et al., 2012].

For the full Iceland graph on 95 individuals, Iceland-1, there is little reduction in the number of graphs. However, for the subset of 31 observed individuals for whom the probability $\mathrm{P}(Y_T|\mathbf{Z};\gamma,\mathbf{\Gamma})$ must be computed (equation (1)), there is a greater than 50-fold reduction even for only 1000 realizations of the IBD graph. When the number of realizations is increased to $30,000$, the speedup is 3 orders of magnitude, while the time to process the IBD graphs increases only from 0.99s to 12.16s. On the single graph of the fglhaps-7 example, there is little reduction from running the software, since there are few marker intervals where the IBD graph is repeated. However, this large is still processed by the software in a relatively negligible 10.39s.

In addition to this, Figure (5) shows the computational results from simulation study of descent of chromosomes of length 10^8 base pairs over multiple population sizes, numbers of realizations, number of generations, and recombination rates. As can be seen, for smaller population sizes, there is a substantial speed improvement, often several orders of magnitude or more. Furthermore, as



(a) Percentage speed improvement by redundant computations eliminated.



(b) Processing time required to compute equivalence classes.

Figure 5: Results showing computation savings in simulated IBD graphs generated from populations of 4,10,20, and 40 individuals (lines), with descent over 5, 10, 50, and 100 generations (columns). The recombination rates per generation are 1.0×10^{-8} per base pair (top rows) and 5.0×10^{-8} (bottom rows), with each individual a pair of chromosomes of length 10^8 base pairs. Results are shown for the IBD graphs of the final generation (x-axes), for sets of 100 to 100,000 realizations

the number of realized IBD graphs in a collection increases, disproportionally more redundancies are found, while the time required to compute the equivalence classes scales linearly. This indicates that even if our method takes several minutes to run – the most time taken in these simulations – it is always worthwhile.

These examples illustrate the power of our framework in working with these types of dynamic data. The advantage of M-Sets and the given operations can be seen easily; many redundant operations can be eliminated. Not surprisingly, these gains are the most substantial on small graphs involving only a few individuals. However, even in the case where there is little reduction (e.g. fglhaps-7), the time taken to process the equivalence classes is negligible relative to the rest of the computations. It should be noted that Iceland-2 and Iceland-3 showed the most dramatic reduction in processing time. The Iceland examples are those where the multiple IBD graphs are realizations estimating a single true latent IBD graph, and are generated conditional on genetic marker data. The variation among graphs is therefore much less than in the independent realizations of descent in the other examples. These Iceland examples demonstrate the significant computational speed-ups that are possible in practice.

8 Conclusion

The representation of objects as hashes permits efficient set operations, which in turn allows many testing algorithms to be expressed in terms of these operations. On more complex data, summarizing and reduction operations allow data types with nested representations to also work with this framework. This is especially true in the target structure, the IBD graph, in which otherwise complex and slow tests can be expressed as simple and intuitive operations. Finally, we showed that real world operations can have substantial speed improvements when using our framework to eliminate redundant operations.

The authors wish to thank Lucas Koepke for his contributions to the code base, Steven Lewis for rigorously testing it, and Chris Glazner for help with the experiments. This open source library is freely available online at `http://www.stat.washington.edu/~hoytak/code/hashreduce`.

Appendix A Hash Function

The Hash function we use is CityHash [Google, 2011], which produces a strong (though not cryptographic) 128 bit hash. We map the resulting hash to $\{0, 1, ..., N\}$, with the upper number chosen to be prime. In our case, we use $N = 2^{128} - 159$ as it is the largest prime that can be represented by a 128 bit integer.

Appendix B Available Operations

We here give a list of operations that are efficiently implemented in our library.

B.1 Validity Set Operations

To work with validity sets, we introduce several operations. These can be broken into two categories, operations that act directly on the validity set of a key and operations that work between validity sets. The former includes operations for constructing and manipulating a validity set, testing whether a key is valid at a given marker value, and iterating through a key's validity set intervals. The latter class implements set operations. These operations all accept keys or a marker validity sets as arguments and return a key or validity set resulting from the respective operation.

IsValid(X, m)
: Returns true if m is a valid point in the validity set or hash object X and false otherwise.

GetVSet(h)
: Returns the validity set of a hash key h.

SetVSet(h, M)
: Sets the validity set of a hash key h to M.

AddVSetInterval(X, a, b), ClearVSetInterval(X, a, b)
: Marks the interval $[a, b)$, $a < b$, as valid or invalid, respectively, in the validity set or hash object X.

VSetUnion(X, Y), VSetIntersection(X, Y), VSetDifference(X, Y)
: Takes the set union, intersection, or difference between two validity sets or hash objects X and Y, returning the result as a hash object if both X and Y are hash objects, and as a validity set otherwise.

VSetMin(X)
: Returns the lowest valid marker value m.

VSetMax(X)
: Returns the greatest marker value m such that there are no valid regions greater than m.

B.2 M-Set Operations

These operations are all efficiently implemented using the previously described algorithms.

B.2.1 Element Operations

Exists(T, k)
: Returns true if a key with hash k exists in T, and false otherwise.

ExistsAt(T, k, m)
: Returns true if a key with hash k exists in T and is valid at marker value m, and false otherwise.

Get(T, k)
: Retrieves any key having hash k from T.

Insert(T, h)
: Inserts the key h into T.

AddValidRegion(T, h, t_1, t_2)
: Sets the region $[t_1, t_2)$ with key h to be valid in T. If h is already present in the table, $[t_1, t_2)$ is set to be valid in that key's V-Set; otherwise, h is given the V-Set $[t_1, t_2)$ and inserted into T.

Pop(T, k)
: Removes any key having hash k from T and returns it.

B.2.2 Hash and Testing Operations

HashAtMarker(T, m)
: Returns the hash formed by Reduce over all the keys valid at marker value m.

EqualAtMarker($T_1, T_2, ..., T_n, m$)
: Returns true if all M-Sets $T_1, T_2, ..., T_n$ contain the same set of keys at marker m, and false otherwise.

EqualityVSet($T_1, T_2, ..., T_n$)
: Returns a marker validity set indicating where all M-Sets are equal.

EqualToHash(T, h)
: Returns a validity set indicating the marker locations on which the reduction of T is equal to the hash h.

B.2.3 Set Operations

Union($T_1, T_2, ..., T_n$)
: Returns an M-Set containing the union over all keys. For each hash value, the new marker validity set is the union of the validity sets of all keys having that key.

Intersection($T_1, T_2, ..., T_n$)
: Returns an M-Set containing the keys present in all input M-Sets, with the new validity set being the intersection of the originals' validity sets. Objects with no valid regions are discarded.

Difference(T_1, T_2)
: Returns an M-Set containing all keys from T_1 with the validity sets from any corresponding hash in T_2 is removed. Keys with empty validity sets are dropped.

B.2.4 Marker Validity Set Operations

MarkerUnion(T, M)
: Returns a new M-Set formed by all the keys in T, where the new validity sets are the union of the original and M.

MarkerIntersection(T, M)
: Returns a new M-Set formed by all the keys in T, where the new validity sets are the intersection of the original and M. Keys with empty validity sets are dropped.

Snapshot(T, m)
: Takes a "snapshot" of the M-Set at a given marker value, returning an M-Set of all the hashes valid at that marker value.

KeySet(T)
: Returns a new M-Set in which all keys in T valid at any marker point in T are returned as an unmarked set. Equivalent to MarkerUnion($T, [-\infty, \infty)$).

UnionOfVSets(T)
: Returns a validity set M formed by taking the union of the validity set of every non-null key present in T.

IntersectionOfVSets(T)
: Returns a validity set M formed by taking the intersection of the validity set of every non-null key present in T.

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